



Quorex Pharmaceuticals

New antimicrobials quiet bacterial talk.

The ability of bacteria to communicate with each other through chemicals was first discovered in the early 1980s. Pathogenic bacteria use this system—so-called quorum sensing—to signal the start of the infection once they have reached a specific density. Several species-specific pathways leading to the release of such chemicals (called autoinducers; AI) were found, but it was not until a signaling system conserved among a range of pathogens—the AI-2 pathway—that researchers saw a means of harnessing quorum sensing for treating bacterial infections. Bonnie Bassler of Princeton University (Princeton, NJ) and Michael Surette of the University of Calgary (Calgary, Alberta, Canada), who discovered AI-1, founded Quorex Pharmaceuticals in early 1999, along with Jeffrey Stein, then principal scientist at Diversa (San Diego, CA), and Bob Robb, manager of a San Diego-based VC fund, BioVentures West.

Quorex owns proprietary technologies, gene sequences and proteins (including the AI-2 molecular structure) that may lead to the identification of new anti-infectives. These drugs are targeted at bacterial surface receptors, preventing them from recognizing autoinducer molecules. This then shuts down the communication pathway that leads to the expression of the pathogen's virulence factors. A secondary result (to be confirmed with additional animal studies) is that the drugs induce a bacteriostatic effect similar to that achieved with chloramphenicol, tetracycline, and erythromycin—the infecting bacteria are unable to obtain nutrients or produce growth factors within the host, and are therefore die or are eliminated by the host's immune system.

New weapons are needed in the fight

against increasing drug resistance among pathogenic bacteria, caused by the over-use of traditional antibiotics. Quorex's quorum-sensing inhibitors could be used against a variety of pathogenic bacteria, including

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Staphylococcus aureus, *Streptococcus pneumoniae*, *E. coli* O157:H7 (the cause of recent outbreaks of serious gastroenteritis), *Haemophilus influenzae*, and *Helicobacter pylori*. Moreover, because the AI-2 pathway is not prevalent in non-pathogenic bacteria, and is absent in higher organisms, drugs will

be both more pathogen-specific and less toxic in humans. The company is also looking at non-quorum-sensing targets—newly discovered bacterial proteins that regulate apoptosis in their (mammalian) cell hosts. Bacterial cells control the cell suicide mechanisms of its host to enable their proliferation. This technology and target family was recently acquired from the Burnham Institute (La Jolla, CA).

Another company currently pursuing similar microbial targets is Aurora Biosciences, which acquired Quorum

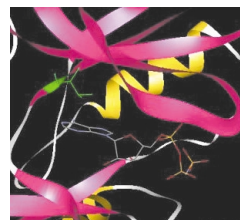
Sciences (Iowa City, IA) in October 2000. However, Quorex has succeeded in attracting an experienced drug development team, led by Krzysztof Appelt, formerly of Agouron and responsible for the development and commercialization of its HIV drug, Viracept. MF

Cellular Genomics

Getting straight to the molecular target.

Swamped with gene sequences, drug companies need fast and accurate ways of validating potential disease targets. In 1998, Yale University's (New Haven, CT) Ira Mellman perceived that advances in cell biology would be necessary to enable genomic-based drug target discovery and validation, and with the help of Yale's Office of Cooperative Research spun off Cellular Genomics.

Most drug discovery companies use small-molecule combinatorial chemistry or various genetic approaches (e.g., antisense



Crystal structure of a kinase with a bound ATP analog.

or gene-knockout technologies) to determine protein function. Louis Matis, Cellular Genomics' president, says that Cellular Genomics brings together the best of both worlds.

The company's proprietary technologies include an analog-sensitive enzyme allele (ASEA) system. The first family of proteins studied using ASEA platform technology are kinases—the enzymes responsible for phosphorylation, and potentially important targets in, for example, cancers and inflammatory disease. Developed by co-founder Kevan Shokat (*Nature* 407, 395, 2000), ASEA can determine not only the physio-

Company: Quorex Pharmaceuticals Inc.

Founded: 1999

Founders: Bonnie Bassler, Robert Robb (chief executive officer), Jeffrey Stein, and Michael Surette

Employees: 8

Financing to date: \$20.7 million

Location: Carlsbad, CA

<http://www.quorex.com>

Founded: 1998

Scientific founders: Ira Mellman, Kevan Shokat, Henrik Dohlman, and Mark Velleca

Employees: 25

Financing to date: \$28 million

Location: Branford, CT

<http://www.cellulargenomics.com>